

1
SEQUENCE LISTING

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<120> HEPARANASE ACTIVITY NEUTRALIZING ANTI- HEPARANASE MONOCLONAL
ANTIBODY AND OTHER ANTI-HEPARANASE ANTIBODIES

<130> 26128

<160> 11

<170> PatentIn version 3.2

<210> 1
<211> 386
<212> PRT
<213> Homo sapiens

<220>
<221> misc feature
<223> 45 kDa subunit of mature processed heparanase dimer

<400> 1

Lys Lys Phe Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu
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Tyr Thr Phe Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn
20 25 30

Ala Leu Leu Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln
35 40 45

Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu
50 55 60

Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile
65 70 75 80

Asn Gly Ser Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu
85 90 95

Arg Lys Ser Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly
100 105 110

Gln Pro Arg Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala
115 120 125

Gly Gly Glu Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn
130 135 140

Gly Arg Thr Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp
145 150 155 160

Ile Phe Ile Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr
165 170 175

Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly
180 185 190

2

Gly Gly Ala Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp
195 200 205

Leu Asp Lys Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met
210 215 220

Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn
225 230 235 240

Phe Asp Pro Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu
245 250 255

Val Gly Thr Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg
260 265 270

Lys Leu Arg Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr
275 280 285

Lys Glu Gly Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr
290 295 300

Lys Tyr Leu Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys
305 310 315 320

Tyr Leu Leu Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val
325 330 335

Gln Leu Asn Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro
340 345 350

Pro Leu Met Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro
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Ala Phe Ser Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala
370 375 380

Cys Ile
385

<210> 2
<211> 535
<212> PRT
<213> Mus musculus

<400> 2

Met Leu Arg Leu Leu Leu Trp Leu Trp Gly Pro Leu Gly Ala Leu
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Ala Gln Gly Ala Pro Ala Gly Thr Ala Pro Thr Asp Asp Val Val Asp
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Leu Glu Phe Tyr Thr Lys Arg Pro Leu Arg Ser Val Ser Pro Ser Phe
35 40 45

Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe Leu
50 55 60

Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu Ser
65 70 75 80

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe
 85 90 95
 Asp Pro Asp Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Lys Ser
 100 105 110
 Gln Val Asn His Asp Ile Cys Arg Ser Glu Pro Val Ser Ala Ala Val
 115 120 125
 Leu Arg Lys Leu Gln Val Glu Trp Pro Phe Gln Glu Leu Leu Leu Leu
 130 135 140
 Arg Glu Gln Tyr Gln Lys Glu Phe Lys Asn Ser Thr Tyr Ser Arg Ser
 145 150 155 160
 Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Gly Leu Asp Leu
 165 170 175
 Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp Asn
 180 185 190
 Ser Ser Asn Ala Gln Leu Leu Leu Asp Tyr Cys Ser Ser Lys Gly Tyr
 195 200 205
 Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys Lys
 210 215 220
 Ala His Ile Leu Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val Glu
 225 230 235 240
 Leu His Lys Leu Leu Gln Arg Ser Ala Phe Gln Asn Ala Lys Leu Tyr
 245 250 255
 Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu Arg
 260 265 270
 Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp His
 275 280 285
 His Tyr Tyr Leu Asn Gly Arg Ile Ala Thr Lys Glu Asp Phe Leu Ser
 290 295 300
 Ser Asp Ala Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu Lys
 305 310 315 320
 Val Thr Lys Glu Ile Thr Pro Gly Lys Lys Val Trp Leu Gly Glu Thr
 325 330 335
 Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe Ala
 340 345 350
 Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Met Gly
 355 360 365
 Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr His
 370 375 380
 Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser Leu
 385 390 395 400

Leu Phe Lys Lys Leu Val Gly Pro Arg Val Leu Leu Ser Arg Val Lys
405 410 415

Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn Val
420 425 430

Tyr His Pro Arg Tyr Gln Glu Gly Asp Leu Thr Leu Tyr Val Leu Asn
435 440 445

Leu His Asn Val Thr Lys His Leu Lys Val Pro Pro Pro Leu Phe Arg
450 455 460

Lys Pro Val Asp Thr Tyr Leu Leu Lys Pro Ser Gly Pro Asp Gly Leu
465 470 475 480

Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Ile Leu Lys Met Val Asp
485 490 495

Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly Ser
500 505 510

Ala Leu Ser Leu Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg Asn
515 520 525

Ala Lys Ile Ala Ala Cys Ile
530 535

<210> 3
<211> 536
<212> PRT
<213> Rattus norvegicus

<400> 3

Met Leu Arg Pro Leu Leu Leu Trp Leu Trp Gly Arg Leu Arg Ala
1 5 10 15

Leu Thr Gln Gly Thr Pro Ala Gly Thr Ala Pro Thr Lys Asp Val Val
20 25 30

Asp Leu Glu Phe Tyr Thr Lys Arg Leu Phe Gln Ser Val Ser Pro Ser
35 40 45

Phe Leu Ser Ile Thr Ile Asp Ala Ser Leu Ala Thr Asp Pro Arg Phe
50 55 60

Leu Thr Phe Leu Gly Ser Pro Arg Leu Arg Ala Leu Ala Arg Gly Leu
65 70 75 80

Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile
85 90 95

Phe Asp Pro Asn Lys Glu Pro Thr Ser Glu Glu Arg Ser Tyr Trp Gln
100 105 110

Ser Gln Asp Asn Asn Asp Ile Cys Gly Ser Glu Arg Val Ser Ala Asp
115 120 125

Val Leu Arg Lys Leu Gln Met Glu Trp Pro Phe Gln Glu Leu Leu Leu
130 135 140

Leu Arg Glu Gln Tyr Gln Arg Glu Phe Lys Asn Ser Thr Tyr Ser Arg
 145 150 155 160
 Ser Ser Val Asp Met Leu Tyr Ser Phe Ala Lys Cys Ser Arg Leu Asp
 165 170 175
 Leu Ile Phe Gly Leu Asn Ala Leu Leu Arg Thr Pro Asp Leu Arg Trp
 180 185 190
 Asn Ser Ser Asn Ala Gln Leu Leu Leu Asn Tyr Cys Ser Ser Lys Gly
 195 200 205
 Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Trp Lys
 210 215 220
 Lys Ala Gln Ile Ser Ile Asp Gly Leu Gln Leu Gly Glu Asp Phe Val
 225 230 235 240
 Glu Leu His Lys Leu Leu Gln Lys Ser Ala Phe Gln Asn Ala Lys Leu
 245 250 255
 Tyr Gly Pro Asp Ile Gly Gln Pro Arg Gly Lys Thr Val Lys Leu Leu
 260 265 270
 Arg Ser Phe Leu Lys Ala Gly Gly Glu Val Ile Asp Ser Leu Thr Trp
 275 280 285
 His His Tyr Tyr Leu Asn Gly Arg Val Ala Thr Lys Glu Asp Phe Leu
 290 295 300
 Ser Ser Asp Val Leu Asp Thr Phe Ile Leu Ser Val Gln Lys Ile Leu
 305 310 315 320
 Lys Val Thr Lys Glu Met Thr Pro Gly Lys Lys Val Trp Leu Gly Glu
 325 330 335
 Thr Ser Ser Ala Tyr Gly Gly Gly Ala Pro Leu Leu Ser Asn Thr Phe
 340 345 350
 Ala Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ser Ala Gln Leu
 355 360 365
 Gly Ile Glu Val Val Met Arg Gln Val Phe Phe Gly Ala Gly Asn Tyr
 370 375 380
 His Leu Val Asp Glu Asn Phe Glu Pro Leu Pro Asp Tyr Trp Leu Ser
 385 390 395 400
 Leu Leu Phe Lys Lys Leu Val Gly Pro Lys Val Leu Met Ser Arg Val
 405 410 415
 Lys Gly Pro Asp Arg Ser Lys Leu Arg Val Tyr Leu His Cys Thr Asn
 420 425 430
 Val Tyr His Pro Arg Tyr Arg Glu Gly Asp Leu Thr Leu Tyr Val Leu
 435 440 445
 Asn Leu His Asn Val Thr Lys His Leu Lys Leu Pro Pro Pro Met Phe

6

450 455 460
 Ser Arg Pro Val Asp Lys Tyr Leu Leu Lys Pro Phe Gly Ser Asp Gly
 465 470 475 480
 Leu Leu Ser Lys Ser Val Gln Leu Asn Gly Gln Thr Leu Lys Met Val
 485 490 495
 Asp Glu Gln Thr Leu Pro Ala Leu Thr Glu Lys Pro Leu Pro Ala Gly
 500 505 510
 Ser Ser Leu Ser Val Pro Ala Phe Ser Tyr Gly Phe Phe Val Ile Arg
 515 520 525
 Asn Ala Lys Ile Ala Ala Cys Ile
 530 535
 <210> 4
 <211> 543
 <212> PRT
 <213> Homo sapiens
 <400> 4
 Met Leu Leu Arg Ser Lys Pro Ala Leu Pro Pro Pro Leu Met Leu Leu
 1 5 10 15
 Leu Leu Gly Pro Leu Gly Pro Leu Ser Pro Gly Ala Leu Pro Arg Pro
 20 25 30
 Ala Gln Ala Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro
 35 40 45
 Leu His Leu Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn
 50 55 60
 Leu Ala Thr Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu
 65 70 75 80
 Arg Thr Leu Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly
 85 90 95
 Thr Lys Thr Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu Ser Thr Phe
 100 105 110
 Glu Glu Arg Ser Tyr Trp Gln Ser Gln Val Asn Gln Asp Ile Cys Lys
 115 120 125
 Tyr Gly Ser Ile Pro Pro Asp Val Glu Glu Lys Leu Arg Leu Glu Trp
 130 135 140
 Pro Tyr Gln Glu Gln Leu Leu Arg Glu His Tyr Gln Lys Lys Phe
 145 150 155 160
 Lys Asn Ser Thr Tyr Ser Arg Ser Ser Val Asp Val Leu Tyr Thr Phe
 165 170 175
 Ala Asn Cys Ser Gly Leu Asp Leu Ile Phe Gly Leu Asn Ala Leu Leu
 180 185 190
 Arg Thr Ala Asp Leu Gln Trp Asn Ser Ser Asn Ala Gln Leu Leu Leu

195	200	205
Asp Tyr Cys Ser Ser Lys Gly Tyr Asn Ile Ser Trp Glu Leu Gly Asn 210 215 220		
Glu Pro Asn Ser Phe Leu Lys Lys Ala Asp Ile Phe Ile Asn Gly Ser 225 230 235 240		
Gln Leu Gly Glu Asp Phe Ile Gln Leu His Lys Leu Leu Arg Lys Ser 245 250 255		
Thr Phe Lys Asn Ala Lys Leu Tyr Gly Pro Asp Val Gly Gln Pro Arg 260 265 270		
Arg Lys Thr Ala Lys Met Leu Lys Ser Phe Leu Lys Ala Gly Gly Glu 275 280 285		
Val Ile Asp Ser Val Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr 290 295 300		
Ala Thr Arg Glu Asp Phe Leu Asn Pro Asp Val Leu Asp Ile Phe Ile 305 310 315 320		
Ser Ser Val Gln Lys Val Phe Gln Val Val Glu Ser Thr Arg Pro Gly 325 330 335		
Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr Gly Gly Gly Ala 340 345 350		
Pro Leu Leu Ser Asp Thr Phe Ala Ala Gly Phe Met Trp Leu Asp Lys 355 360 365		
Leu Gly Leu Ser Ala Arg Met Gly Ile Glu Val Val Met Arg Gln Val 370 375 380		
Phe Phe Gly Ala Gly Asn Tyr His Leu Val Asp Glu Asn Phe Asp Pro 385 390 395 400		
Leu Pro Asp Tyr Trp Leu Ser Leu Leu Phe Lys Lys Leu Val Gly Thr 405 410 415		
Lys Val Leu Met Ala Ser Val Gln Gly Ser Lys Arg Arg Lys Leu Arg 420 425 430		
Val Tyr Leu His Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys Glu Gly 435 440 445		
Asp Leu Thr Leu Tyr Ala Ile Asn Leu His Asn Val Thr Lys Tyr Leu 450 455 460		
Arg Leu Pro Tyr Pro Phe Ser Asn Lys Gln Val Asp Lys Tyr Leu Leu 465 470 475 480		
Arg Pro Leu Gly Pro His Gly Leu Leu Ser Lys Ser Val Gln Leu Asn 485 490 495		
Gly Leu Thr Leu Lys Met Val Asp Asp Gln Thr Leu Pro Pro Leu Met 500 505 510		

8

Glu Lys Pro Leu Arg Pro Gly Ser Ser Leu Gly Leu Pro Ala Phe Ser
 515 520 525

Tyr Ser Phe Phe Val Ile Arg Asn Ala Lys Val Ala Ala Cys Ile
 530 535 540

<210> 5
 <211> 523
 <212> PRT
 <213> Gallus gallus

<400> 5

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Arg Thr Ala Glu Leu Gln Leu Gly Leu Arg Glu Pro Ile Gly Ala Val
 20 25 30

Ser Pro Ala Phe Leu Ser Leu Thr Leu Asp Ala Ser Leu Ala Arg Asp
 35 40 45

Pro Arg Phe Val Ala Leu Leu Arg His Pro Lys Leu His Thr Leu Ala
 50 55 60

Ser Gly Leu Ser Pro Gly Phe Leu Arg Phe Gly Gly Thr Ser Thr Asp
 65 70 75 80

Phe Leu Ile Phe Asn Pro Asn Lys Asp Ser Thr Trp Glu Glu Lys Val
 85 90 95

Leu Ser Glu Phe Gln Ala Lys Asp Val Cys Glu Ala Trp Pro Ser Phe
 100 105 110

Ala Val Val Pro Lys Leu Leu Leu Thr Gln Trp Pro Leu Gln Glu Lys
 115 120 125

Leu Leu Leu Ala Glu His Ser Trp Lys Lys His Lys Asn Thr Thr Ile
 130 135 140

Thr Arg Ser Thr Leu Asp Ile Leu His Thr Phe Ala Ser Ser Ser Gly
 145 150 155 160

Phe Arg Leu Val Phe Gly Leu Asn Ala Leu Leu Arg Arg Ala Gly Leu
 165 170 175

Gln Trp Asp Ser Ser Asn Ala Lys Gln Leu Leu Gly Tyr Cys Ala Gln
 180 185 190

Arg Ser Tyr Asn Ile Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe
 195 200 205

Arg Lys Lys Ser Gly Ile Cys Ile Asp Gly Phe Gln Leu Gly Arg Asp
 210 215 220

Phe Val His Leu Arg Gln Leu Leu Ser Gln His Pro Leu Tyr Arg His
 225 230 235 240

Ala Glu Leu Tyr Gly Leu Asp Val Gly Gln Pro Arg Lys His Thr Gln
 245 250 255

9

His Leu Leu Arg Ser Phe Met Lys Ser Gly Gly Lys Ala Ile Asp Ser
 260 265 270
 Val Thr Trp His His Tyr Tyr Val Asn Gly Arg Ser Ala Thr Arg Glu
 275 280 285
 Asp Phe Leu Ser Pro Glu Val Leu Asp Ser Phe Ala Thr Ala Ile His
 290 295 300
 Asp Val Leu Gly Ile Val Glu Ala Thr Val Pro Gly Lys Lys Val Trp
 305 310 315 320
 Leu Gly Glu Thr Gly Ser Ala Tyr Gly Gly Gly Ala Pro Gln Leu Ser
 325 330 335
 Asn Thr Tyr Val Ala Gly Phe Met Trp Leu Asp Lys Leu Gly Leu Ala
 340 345 350
 Ala Arg Arg Gly Ile Asp Val Val Met Arg Gln Val Ser Phe Gly Ala
 355 360 365
 Gly Ser Tyr His Leu Val Asp Ala Gly Phe Lys Pro Leu Pro Asp Tyr
 370 375 380
 Trp Leu Ser Leu Leu Tyr Lys Arg Leu Val Gly Thr Arg Val Leu Gln
 385 390 395 400
 Ala Ser Val Glu Gln Ala Asp Ala Arg Arg Pro Arg Val Tyr Leu His
 405 410 415
 Cys Thr Asn Pro Arg His Pro Lys Tyr Arg Glu Gly Asp Val Thr Leu
 420 425 430
 Phe Ala Leu Asn Leu Ser Asn Val Thr Gln Ser Leu Gln Leu Pro Lys
 435 440 445
 Gln Leu Trp Ser Lys Ser Val Asp Gln Tyr Leu Leu Leu Pro His Gly
 450 455 460
 Lys Asp Ser Ile Leu Ser Arg Glu Val Gln Leu Asn Gly Arg Leu Leu
 465 470 475 480
 Gln Met Val Asp Asp Glu Thr Leu Pro Ala Leu His Glu Met Ala Leu
 485 490 495
 Ala Pro Gly Ser Thr Leu Gly Leu Pro Ala Phe Ser Tyr Gly Phe Tyr
 500 505 510
 Val Ile Arg Asn Ala Lys Ala Ile Ala Cys Ile
 515 520
 <210> 6
 <211> 10
 <212> PRT
 <213> Artificial sequence
 <220>
 <223> Functional peptide epitope of heparanase
 <400> 6
 Cys Thr Asn Thr Asp Asn Pro Arg Tyr Lys

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10
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<210> 7
<211> 19
<212> PRT
<213> Artificial sequence

<220>
<223> Functional peptide epitope of heparanase

<400> 7

Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr Asp Phe Leu Ile Phe
1          5          10          15

Asp Pro Lys

<210> 8
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> Functional peptide epitope of heparanase

<400> 8

Ser Trp Glu Leu Gly Asn Glu Pro Asn Ser Phe Leu Lys Lys Ala
1          5          10          15

<210> 9
<211> 15
<212> PRT
<213> Artificial sequence

<220>
<223> Functional peptide epitope of heparanase

<400> 9

Arg Pro Gly Lys Lys Val Trp Leu Gly Glu Thr Ser Ser Ala Tyr
1          5          10          15

<210> 10
<211> 14
<212> PRT
<213> Artificial sequence

<220>
<223> Functional peptide epitope of heparanase

<400> 10

Thr Trp His His Tyr Tyr Leu Asn Gly Arg Thr Ala Thr Arg
1          5          10

<210> 11
<211> 74
<212> PRT
<213> Homo sapiens

<220>
<221> misc_feature
<223> 8 kDa subunit of mature processed heparanase dimer

<400> 11

Gln Asp Val Val Asp Leu Asp Phe Phe Thr Gln Glu Pro Leu His Leu
1          5          10          15

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11

Val Ser Pro Ser Phe Leu Ser Val Thr Ile Asp Ala Asn Leu Ala Thr
20 25 30

Asp Pro Arg Phe Leu Ile Leu Leu Gly Ser Pro Lys Leu Arg Thr Leu
35 40 45

Ala Arg Gly Leu Ser Pro Ala Tyr Leu Arg Phe Gly Gly Thr Lys Thr
50 55 60

Asp Phe Leu Ile Phe Asp Pro Lys Lys Glu
65 70